In the Claims

1-2. (Cancel)

3. (Amended) An isolated polynucleotide that encodes a polypeptide ~~according to claim 1~~ comprising SEQ ID NO:16 or a truncated portion thereof of at least 50 amino acid residues wherein said portion retains the ability to enhance ubiquitination of phosphorylated lkB~~, wherein the polynucleotide does not encode a full-length human E3 ubiquitin ligase~~.

4. (Cancel)

5. An antisense polynucleotide comprising at least 10 consecutive nucleotides complementary to a polynucleotide according to claim 3.

6. (Amended) An expression vector comprising a polynucleotide according to ~~any one of claims 3-5~~ claim 3.

7. A host cell transformed or transfected with an expression vector according to claim 6.

8. (Amended) A pharmaceutical composition, comprising:

(a) an isolated human E3 ubiquitin ligase polypeptide~~, wherein the polypeptide comprises a sequence recited in SEQ ID NO: 16, or a truncated version of SEQ ID NO:16 at least about 50 residues in length that differs no more than 15% in identity and position to the residues in SEQ ID NO:16~~ comprising SEQ ID NO:16 or a truncated portion thereof of at least 50 amino acid residues wherein said portion retains the ability to enhance ubiquitination of phosphorylated lkB, such that the polypeptide enhances ubiquitination of phosphorylated IκB; and

(b) a physiologically acceptable carrier.

9. (Cancel)

10. (Amended) A pharmaceutical composition, comprising:

(a) an isolated human E3 ubiquitin ligase polypeptide~~, wherein the polypeptide comprises SEQ ID NO: 16, or a truncated version of SEQ ID NO:16 at least about 50 residues in length that differs no more than 15% in identity and position to the residues in SEQ ID NO: 16, such that the polypeptide binds to phosphorylated IκB and inhibits ubiquitination of phosphorylated IκB~~ comprising a truncated portion of SEQ ID NO:16 comprising from 50 to 250 residues of SEQ ID NO:16 wherein said portion retains the ability to bind to phosphorylated lkB and inhibits ubiquitination of phosphorylated lkB; and

(b) a physiologically acceptable carrier.

11-12. (Cancel)

13. An isolated antibody, or antigen binding fragment thereof, that binds to a human E3 ubiquitin ligase sequence recited in SEQ ID NO: 16.

14. An antibody or fragment thereof according to claim 13, wherein the antibody is a monoclonal antibody.

15. A pharmaceutical composition comprising an antibody or fragment thereof according to claim 13, in combination with a physiologically acceptable carrier.

16. (Amended) A method for modulating NF - κB activity in a patient, comprising administering to a patient a pharmaceutical composition according to [[any one of claims 8-9]] claim 8 or claim 9 and thereby modulating NF - κB activity in the patient.

17. (Cancel)

18. (Amended) A method according to claim [[17]] 16, wherein the disorder is selected from the group consisting of inflammatory diseases, autoimmune diseases, cancer and viral infection.

19. (Amended) A method for screening for an agent that modulates NF- κB activity, comprising the steps of:

(a) contacting a candidate agent with an isolated human E3 ubiquitin ligase polypeptide [[according to any one of claims 1-2 or 26-34]] comprising SEQ ID NO:16 or a truncated portion thereof of at least 50 amino acid residues wherein said portion retains the ability to enhance ubiquitination of phosphorylated IkB, under conditions and for a time sufficient to permit interaction between the polypeptide and candidate agent; and

(b) subsequently evaluating the ability of the polypeptide to enhance ubiquitination of phosphorylated IκB, relative to a predetermined ability of the polypeptide to enhance ubiquitination of phosphorylated IκB in the absence of the candidate agent [[modulate NF- κB activity]].

20. A method according to claim 19, wherein the candidate agent is a small molecule.

21-25. (Cancel)

26. (New) A method for screening for an agent that modulates NF- κB activity, comprising the steps of:

(a) contacting a candidate agent with an isolated human E3 ubiquitin ligase polypeptide [[according to any one of claims 1 or 26-30]] comprising a variant of SEQ ID NO:16 that differs therefrom at no more than 10% of the amino acid residues of SEQ ID NO:16 wherein said variant retains the ability to enhance ubiquitination of phosphoylated IkB, under conditions and for a time sufficient to permit interaction between the polypeptide and candidate agent; and

(b) subsequently evaluating the ability of the polypeptide to enhance ubiquitination of phosphorylated IκB, relative to a predetermined ability

of the polypeptide to enhance ubiquitination of phosphorylated IκB in the absence of the candidate agent; and therefrom identifying an agent that modulates NF- κB activity.

27. (New) A method for screening for an agent that modulates NF- κB activity, comprising the steps of:

(a) contacting a candidate agent with an isolated human E3 ubiquitin ligase polypeptide [[according to any one of claims 1-2 or 26-34]] comprising SEQ ID NO:16 or a truncated portion thereof of at least 50 amino acid residues wherein said portion retains the ability to enhance ubiquitination of phosphorylated IkB, under conditions and for a time sufficient to permit interaction between the polypeptide and candidate agent; and

(b) subsequently evaluating the ability of the polypeptide to bind phosphorylated IκB or a phosphorylated IκB peptide comprising SEQ ID NO:8 or SEQ ID NO:9; and therefrom identifying an agent that modulates NF- κB activity.

28. (New) A method for screening for an agent that modulates NF- κB activity, comprising the steps of:

(a) contacting a candidate agent with an isolated human E3 ubiquitin ligase polypeptide [[according to any one of claims 1-2 or 26-34]] comprising SEQ ID NO:16 or a truncated portion thereof of at least 50 amino acid residues wherein said portion retains the ability to enhance ubiquitination of phosphorylated IkB, under conditions and for a time sufficient to permit interaction between the polypeptide and candidate agent; and

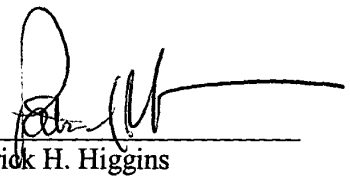
(b) subsequently evaluating the ability of the polypeptide to modulate the release NF- κB from IκB or the nuclear translocation of NF- κB; and therefrom identifying an agent that modulates NF- κB activity.

* * *

The Examiner is kindly encouraged to telephone the undersigned in order to expedite any detail of the prosecution.

The Commissioner is authorized to charge any deficiency or credit any overpayment in connection herewith to Deposit Account No. 13-2165.

Respectfully submitted,



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